

04 Out
within the 300 base pair element of the tyrosinase promoter, plasmids were made in which the HSE element was separated from the C nucleotide at position -300 of the Tyr-300 promoter by either no nucleotides or one full turn of the DNA helix (HSE-Tyr 300-FULL) or by a stuffer fragment representing one half turn of the helix (HSE Tyr-300-HALF) (Figure 10A). Both HSE-Tyr 300-GM-CSF plasmids transfected into MeWo melanoma cells produced the same low levels of GM-CSF as the Tyr300-GM-CSF plasmid (Figure 10B). However, when the transfected cells were heat shocked 42°C for 30 minutes, 24 hours following transfection, GM-CSF production was increased, but only in cells transfected with the HSE-Tyr300 plasmids (Figure 10B). --

In the claims:

Please cancel claims 1-8, 10-14, and 16-33 without prejudice.

Please amend claims 9 and 15 as follows:

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--9. (Amended Once) A composition comprising nucleic acid, wherein said nucleic acid comprises:

(a) a cell type-specific promoter for activating the expression of a gene in a specific cell type, wherein the cell type-specific promoter is human Tyr300 (SEQ ID. NO. 1);

(b) a therapeutic gene sequence operably linked to said cell type-specific promoter;

(c) an amplification promoter element for amplifying transcription of said therapeutic gene in said specific cell type; and

(d) a sequence encoding a transcription activator, said transcription activator for activating said amplification promoter element.

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15. (Amended Once) A composition comprising nucleic acid, wherein said nucleic acid comprises:

(a) a cell type-specific promoter for activating the expression of a gene in a specific cell type;

(b) a therapeutic gene sequence operably linked to said cell type-specific promoter;

(c) an amplification promoter element for amplifying transcription of said therapeutic gene in said specific cell type; and

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ent

(d) a sequence encoding a transcription activator, said transcription activator for activating said amplification promoter element, wherein said nucleic acid produces a level of mRNA expression which is at least 100-fold higher in *in vitro* cells of the specific cell type compared to *in vitro* cells which are not of the specific cell type.--

Please add claims 34-66 as follows:

-- 34. (New) The composition of claim 9, wherein said amplification promoter element is a stress inducible promoter element. B

35. (New) The composition of claim 9, wherein said sequence encoding said transcription activator sequence and said therapeutic gene sequence are on different nucleic acid molecules.

36. (New) The composition of claim 9, wherein said amplification promoter element is a heat shock element. B

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37. (New) The composition of claim 9, wherein said amplification promoter element comprises at least one human HSE consensus sequence.

38. (New) The composition of claim 9, wherein said therapeutic gene is a cytotoxic gene.

39. (New) The composition of claim 38, wherein said cytotoxic gene encodes a fusogenic protein.

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40. (New) The composition of claim 38, wherein the cytotoxic gene is GALVenv, HSVTK, cytosine deaminase, nitroreductase, or VSV-G glycoprotein.

41. (New) The composition of claim 9, wherein said nucleic acid produces a level of mRNA expression which is at least 100-fold higher in *in vitro* cells of the specific cell type compared to *in vitro* cells which are not of the specific cell type.

42. (New) The composition of claim 9, wherein said nucleic acid produces a level of therapeutic gene mRNA expression which is at least 500-fold higher in *in vitro* cells of the specific cell type compared to *in vitro* cells which are not of the specific cell type.

Rule 126
~~42~~⁴³. (New) The composition of claim 9, wherein said nucleic acid produces a level of therapeutic gene mRNA expression which is at least 1000-fold higher in *in vitro* cells of the specific cell type compared to *in vitro* cells which are not of the specific cell type.

Rule 126
~~43~~⁴⁴. (New) The composition of claim 9, wherein said amplification promoter element is an HSE, and wherein said transcription activator is HSF-1.

Rule 126
~~44~~⁴⁵. (New) The composition of claim 9, wherein said transcription activator is activateable by a stressor.

Rule 126
~~45~~⁴⁶. (New) The composition of claim 9, wherein said transcription activator is constitutively expressed.

Rule 126
~~46~~⁴⁷. (New) The composition of claim 9, wherein said therapeutic gene and said transcription activator are both operably linked to said cell type-specific promoter.

Rule 126
~~47~~⁴⁸. (New) The composition of claim 9, wherein said therapeutic gene and said transcription activator are both operably linked to said amplification promoter element.

Rule 126
~~48~~⁴⁹. (New) The composition of claim 9, wherein said transcription activator is HSF-1 comprising a deletion of amino acid residues 202-316.

Rule 126
~~49~~⁵⁰. (New) The composition of claim 15, wherein said cell type-specific promoter is a tissue-specific promoter.

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~~50.~~ (New) The composition of claim 15, wherein said cell type-specific promoter is a tumor-specific promoter.

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~~51.~~ (New) The composition of claim 15, wherein said amplification promoter element is a stress inducible promoter element.

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~~52.~~ (New) The composition of claim 15, wherein said sequence encoding said transcription activator sequence and said therapeutic gene sequence are on different nucleic acid molecules.

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~~53.~~ (New) The composition of claim 15, wherein said cell type-specific promoter element is a heat shock element.

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~~54.~~ (New) The composition of claim 15, wherein said cell type-specific promoter is human Tyr300 (SEQ ID NO: 1).

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~~55.~~ (New) The composition of claim 15, wherein said amplification promoter element comprises at least one human HSE consensus sequence.

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~~56.~~ (New) The composition of claim 15, wherein said therapeutic gene is a cytotoxic gene.

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~~57.~~ (New) The composition of claim ~~56~~⁵⁷, wherein said cytotoxic gene encodes a fusogenic protein.

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~~58.~~ (New) The composition of claim ~~56~~⁵⁷, wherein the cytotoxic gene is GALVenv, HSVTK, cytosine deaminase, nitroreductase, or VSV-G glycoprotein.

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~~59.~~ (New) The composition of claim 15, wherein said nucleic acid produces a level of therapeutic gene mRNA expression which is at least 500-fold higher in *in vitro* cells of the specific cell type compared to *in vitro* cells which are not of the specific cell type.

Rule 126
~~61~~
61. (New) The composition of claim 15, wherein said nucleic acid produces a level of therapeutic gene mRNA expression which is at least 1000-fold higher in *in vitro* cells of the specific cell type compared to *in vitro* cells which are not of the specific cell type.

Rule 126
~~62~~
62. (New) The composition of claim 15, wherein said amplification promoter element is an HSE, and wherein said transcription activator is HSF-1.

Rule 126
~~63~~
63. (New) The composition of claim 15, wherein said transcription activator is activateable by a stressor. *B*

Rule 126
~~64~~
64. (New) The composition of claim 15, wherein said transcription activator is constitutively expressed.

Rule 126
~~65~~
65. (New) The composition of claim 15, wherein said therapeutic gene and said amplification promoter element are both operably linked to said cell type-specific promoter.

Rule 126
~~66~~
66. (New) The composition of claim 15, wherein said therapeutic gene and said transcription activator are both operably linked to said amplification promoter element.

Rule 126
~~67~~
67. (New) The composition of claim 15, wherein said transcription activator is HSF-1 comprising a deletion of amino acid residues 202-316. --